

NCEA CLEARANCE FORM FOR STICS APPLICATION

Product Information:		*Product Category (Select one):	
Clearance Tracking Number:		<input type="checkbox"/> HISA (Highly Influential Scientific Assessment) <input type="checkbox"/> ISI (Influential Scientific Information) <input type="checkbox"/> High Profile and/or Policy Relevant (not HISA or ISI) <input checked="" type="checkbox"/> Other	
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*Product Type:	Journal article		
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Key Characteristics of Carcinogens and Approaches to using Mechanistic Data in their Classification			
Principal Investigator/Project Officer Information:		EPA Author: If same as PI, check box: <input type="checkbox"/>	
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*Impact/Purpose Statement:			
A Working Group of experts convened by the International Agency for Research on Cancer identified 10 key characteristics that are commonly exhibited by agents that are known to be carcinogenic to humans. This manuscript discusses these key characteristics and shows how they can be used in a systematic review and subsequent cancer classification. This work will be useful in the EPA's IRIS program in evaluations of mechanistic studies.			
*Product Description/Abstract:			
A recent review by the International Agency for Research on Cancer (IARC) updated the assessments of the more than 100 agents classified as established Group 1 human carcinogens (IARC Monographs Volume 100). This exercise was complicated by the absence of a broadly accepted, systematic method for evaluating mechanistic data to support conclusions regarding human risk from exposure to carcinogens. IARC therefore sponsored two workshops in which an international Working Group of experts identified 10 key characteristics, one or more of which are commonly exhibited by established human carcinogens. These characteristics provide the basis for an objective approach to identifying and organizing results from pertinent mechanistic studies. The ten characteristics are the abilities of an agent to: (1) act as an electrophile either directly or after metabolic activation; (2) be genotoxic; (3) alter DNA repair or cause genomic instability; (4) induce epigenetic alterations; (5) induce oxidative stress; (6) induce chronic inflammation; (7) be immunosuppressive; (8) modulate receptor-mediated effects; (9) cause immortalization; and, (10) alter cell proliferation, cell death, or nutrient supply. We describe the use of the 10 key characteristics to conduct a systematic literature search focused on relevant endpoints and construct a graphical representation of the identified mechanistic information. Next, we use a number of Group 1 carcinogens as examples, to illustrate how this approach may work in practice. The approach described is similar to that currently being developed and implemented by the U.S. EPA's IRIS Program and the U.S. National Toxicology Program.			
*Tracking and Planning: Planning data may be obtained from the Research Management System (RMS). The link to the website is: http://v26265ncay506.aa.ad.epa.gov/rms/RMSPortfolio.cfm.			

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Bibliographic Citation Components:			
*Meeting Name:		*Meeting City:	
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*Meeting End Date:		*Meeting Country:	
*Journal:	Carcinogenesis (proposed)	URL:	
*Access:		*Copyright Permission:	
<input type="checkbox"/> EPA Only <input checked="" type="checkbox"/> Public		<input type="checkbox"/> Yes (Permission Attached) <input type="checkbox"/> No <input type="checkbox"/> Not Applicable	
*Quality Assurance:		*Policy Implications:	
Is a form indicating QA approval for this product attached?		This product enunciates new policy or affects existing policy?	
<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not Applicable		<input type="checkbox"/> Yes (Memo Attached) <input checked="" type="checkbox"/> No	
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2.Mechanisms		5.	
3.Systematic review		6.	
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*Completion is required.